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10/552,159	12/08/2006	Daksh Sadarangani	87036-0005	9207

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EXAMINER	
BERTAGNA, ANGELA MARIE	
ART UNIT	**PAPER NUMBER**
1637	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/552,159	SADARANGANI ET AL.	
	Examiner	Art Unit	
	ANGELA BERTAGNA	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 December 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *58-82* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *58-82* is/are rejected.

7)☒ Claim(s) *59-61,64-67,72,73,75,80 and 81* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11 October 2005* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/31/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

1. Applicant's response filed on December 31, 2008 is acknowledged. Claims 58-82 are currently pending. In the response, Applicant canceled all of the previously presented claims (*i.e.* claims 1-25) and presented new claims 58-82.

All of the previously made objections and rejections have been obviated by Applicant's cancellation of all of the previously examined claims and the presentation of new claims 58-82. The following are new grounds of rejection. The new grounds of rejection presented below were necessitated by Applicant's amendments to the claims and submission of an Information Disclosure Statement on December 31, 2008. Accordingly, this Office Action is made **FINAL**.

Priority

2. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Information Disclosure Statement

3. Applicant's submission of an information disclosure statement on December 31, 2008 is acknowledged. A signed copy is enclosed.

Drawings

4. The drawings are objected to as failing to comply with 37 CFR 1.84(p)(5) because they do not include the following reference sign(s) mentioned in the description: **60**. Corrected

drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

The drawings are objected to as failing to comply with 37 CFR 1.84(p)(5) because they include the following reference character(s) not mentioned in the description: **50**. Corrected drawing sheets in compliance with 37 CFR 1.121(d), or amendment to the specification to add the reference character(s) in the description in compliance with 37 CFR 1.121(b) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Claim Objections

5. Claim 59 is objected to because of the following informalities: Deleting the comma after the word "housing" in line 2 is suggested to improve the clarity of the claim.

Claims 60 and 61 are objected to because of the following informalities: These claims contain a typographical error where "M_gCl_2" is recited.

Claim 64 is objected to because of the following informalities: The recitation "replacements tips" is grammatically incorrect. Also, deletion of the comma following the words "heating element" is suggested to improve the clarity of the claim.

Claim 65 is objected to because of the following informalities: Replacing "the media" in part (a) with "the gel filtration media" is suggested to improve consistency within the claim.

Claim 66 is objected to because of the following informalities: This claim appears to be missing the word "to" after the word "controlling" in line 2.

Claim 67 is objected to because of the following informalities: This claim contains a typographical error where "argose" is recited.

Claims 72 and 73 are objected to because of the following informalities: These claims contain a typographical error where "complimentary" is recited.

Claim 75 is objected to because of the following informalities: This claim appears to be missing the word "a" before the word "dye" in part b.

Claim 80 is objected to because of the following informalities: Replacing "the fragments" in line 2 with "the DNA fragments" is suggested to improve consistency within the claim.

Claim 81 is objected to because of the following informalities: This claim contains a typographical error in line 1 where "said the reader" is recited.

Claim Rejections - 35 USC § 112, 2nd paragraph

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 60, 61, 64, 67-70, and 72-82 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 60 and 61 are indefinite, because they recite the limitations "the extraction solution containing proteinase and 100 microliters of buffer solution for each microliter or proteinase" and "the master solution containing a buffer, a Taq DNA polymerase, two oligonucleotide primers, deoxynucleoside triphosphate, and $MgCl_2$". There is insufficient antecedent basis for these limitations in the claims. There is sufficient antecedent basis for "the extraction solution" and "the master solution", respectively.

Claim 64 is indefinite, because there is insufficient antecedent basis for the limitation "the reservoirs for various solutions", which appears in lines 2-3.

Claim 67 is indefinite, because there is insufficient antecedent basis for the limitation "each DNA fragment", which appears in lines 3-4.

Claim 68 is indefinite, because there is insufficient antecedent basis for the limitation "the fragments", which appears in lines 3-4.

Claims 69 and 70 are indefinite, because there is insufficient antecedent basis for the limitation "the cells", which appears in part (a). Claims 69 and 70 are also indefinite, because they depend from claim 60, which is indefinite.

Claims 72-74 are indefinite, because they depend from claim 60, which is indefinite (see above).

Claim 75 is indefinite, because there is insufficient antecedent basis for the limitation "the gel filtration media", which appears in part (a).

Claims 76-78 are indefinite, because they depend from claim 75, which is indefinite (see above).

Claims 78 is further indefinite, because there is insufficient antecedent basis for the limitation "the electrophoresis equipment", which appears in line 2.

Claim 79 is indefinite, because it recites the limitations "said voltage source" in line 1, "the DNA fragments" in line 2, and "the electrophoresis equipment" in line 2. There is insufficient antecedent basis for these limitations in the claim.

Claims 80-82 are indefinite, because they depend from claim 67, which is indefinite (see above).

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 58-65, 67-74, and 79-82 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chan et al. (WO 2000/60362 A1; cited on the IDS filed on December 31, 2008) in view of Belgrader et al. (Laboratory Research and Automation (1997) 9: 3-7; cited previously) as evidenced by the ABI Prism 310 Genetic Analyzer User's Manual (1998; cited previously) and further in view of Nix et al. (US 6,402,950 B1).

These claims are drawn to a DNA analysis system.

Regarding claim 58, Chan teaches a DNA analysis system comprising the following elements (see Figure 1, pages 5-7, and pages 11-23): a housing, a receptacle, a plurality of reservoirs, a pipette, a control arrangement for controlling movement of a sample between the reservoirs, a heating element, a controller, a microcontroller, an electrophoresis device, a reader, and a computer. Chan further teaches that the disclosed apparatus can be customized such that the three subsystems comprising the apparatus (*i.e.* the extraction subsystem, the amplification subsystem, and the electrophoresis subsystem) can be removed to permit updating and/or expansion (see abstract and page 5).

Regarding claim 59, in the apparatus of Chan, the receptacle (*i.e.* the plate holder) is mounted on top of the housing and contains the plurality of reservoirs (*i.e.* the microplate) (see Figure 1).

Regarding claims 60 and 61, the reservoirs in the apparatus of Chan (*i.e.* the wells of the microplate) contain the sample, an extraction solution comprising a buffer and a proteinase, and a PCR master solution comprising a Taq DNA polymerase, two oligonucleotide primers, a buffer, dNTPs, and $MgCl_2$ (see pages 26-27, for example).

Regarding claims 62 and 63, in the apparatus of Chan, the control arrangement comprises a beam and an arm that is suspended from the beam and displaceable horizontally along the beam (see Figure 1 and pages 19 and 23). In the apparatus of Chan, the pipette is mounted to the arm (see Figure 1 and pages 19 and 23).

Regarding claim 64, the apparatus of Chan comprises a holder for holding replacement pipette tips that is located adjacent to the heating element and contains reservoirs for holding a plurality of solutions (see Figure 1 and pages 5, 19, and 22).

Regarding claims 69, 70, and 72-74, Chan teaches that the apparatus contains a plurality of computer-controlled incubators (pages 6 and 13-14). Chan also teaches that the thermal cycler is programmed such that the heating element heats the sample at 94°C for 30 minutes followed by 35 cycles of 94°C for 60 seconds, 55°C for 60 seconds, and 72°C for 60 seconds followed by 72°C for 10 minutes (see page 27). Chan further teaches that the system should be programmed as desired by the user to obtain the desired reaction parameters (*i.e.* incubation at a particular temperature for a given time) (see pages 20-21).

Regarding claim 71, in the apparatus of Chan the controller is inherently capable of causing the pipette to mix the PCR master solution with the sample and extraction solution to create a combined solution.

Regarding claim 79, the apparatus of Chan includes a voltage source that is inherently capable of subjecting a combination of the sample, extraction solution, and PCR master solution to a high voltage field to cause DNA fragments to migrate through the electrophoresis device (see Figure 1 and pages 18, 27, and 28).

The DNA analysis system of Chan does not include a gel filtration device as required by claims 58 and 65. Also, the extraction buffer included in the DNA analysis system of Chan does not contain a buffer and proteinase in the proportions recited in claim 61. The DNA analysis system of Chan also does not include a capillary electrophoresis device having the features recited in claims 67, 68, and 80-82. Finally, the apparatus of Chan does not have a microcontroller programmed as required by claims 69-74.

Belgrader teaches a DNA analysis system for conducting nucleic acid extraction, PCR amplification, and capillary electrophoresis (see abstract and pages 4-5). Belgrader teaches that capillary electrophoresis analysis is "an attractive replacement for slab gel electrophoresis since runs can be accomplished much faster, and gel casting and manual sample loading are eliminated (page 3, column 2).

Regarding claim 58, the DNA analysis system of Belgrader comprises the following elements (see Figure 1 and pages 4-5): a housing, a receptacle, a plurality of reservoirs, a pipette, a control arrangement for controlling movement of the sample between reservoirs, a heating element, a controller, a microcontroller, an electrophoresis device, a computer, and a reader.

Regarding claim 59, in the apparatus of Belgrader, the receptacle (*i.e.* the plate holder) is mounted on top of the housing and contains the plurality of reservoirs (*i.e.* the microplate) (see Figure 1).

Regarding claims 60 and 61, the reservoirs in the apparatus of Belgrader (*i.e.* the wells of the microplate) contain the sample, an extraction solution, and a PCR master solution comprising a Taq DNA polymerase, two oligonucleotide primers, a buffer, dNTPs, and $MgCl_2$ (page 4).

Regarding claims 67 and 79-82, as evidenced by the ABI Prism Genetic Analyzer 310 User's manual at pages 1-2 -> 1-12, for example, the electrophoresis device in the apparatus of Belgrader includes a capillary containing a polyacrylamide gel, a high voltage source, a laser, and a detector. In the apparatus of Belgrader, the voltage source is inherently capable of subjecting a combination of the sample, extraction solution, and PCR master solution to a high voltage field to cause DNA fragments to migrate through the electrophoresis device. Also, the detector in the apparatus of Belgrader is inherently capable of causing the laser to emit light onto DNA fragments to cause the DNA fragments to emit light. Also, the reader in the apparatus of Belgrader is inherently capable of capturing images of the light emitted from the DNA fragments and outputting the images to the computer. Finally, in the apparatus of Belgrader, the computer uses software to convert the images into an electropherogram that is displayed on the monitor.

Regarding claim 68, as evidenced by the teachings of the ABI PRISM Genetic Analyzer 310 User's manual at page 1-2, for example, reader in the apparatus of Belgrader is capable of reading fluorescent ends of nucleic acid fragments and comprises a CCD camera that outputs captured images into a monitoring means.

Regarding claim 71, in the apparatus of Belgrader the controller is capable mixing the PCR master solution with the sample and extraction solution to create a combined solution.

Regarding claims 72-74, Belgrader teaches that the thermal cycler is programmed such that the heating element heats the sample at 96°C for 2 minutes followed by 10 cycles of 94°C

for 30 seconds, 60°C for 30 seconds, and 70°C for 30 seconds followed by 20 cycles of 90°C for 30 seconds, 60°C for 30 seconds, 70°C for 30 seconds, and 70°C for 10 minutes (see page 4, column 2).

The DNA analysis system of Belgrader does not include a gel filtration device as required by claim 58.

Nix teaches that methods and devices for conducting gel filtration (see abstract and column 3, lines 39-55). Nix teaches that gel filtration is useful for removing salts and buffers from samples prior to conducting capillary electrophoresis (column 2, lines 41-53). Regarding claim 65, the gel filtration device taught by Nix comprises a tube filled with gel filtration media that permits large DNA fragments to pass through the media before smaller fragments or unwanted substances can pass through the media and a downstream end for collecting larger fragments of DNA (see Figures 1-4 and column 3, line 55 – column 4, line 21 and column 7, line 28 – column 8, line 48).

It would have been *prima facie* obvious for one of ordinary skill in the art at the time of invention to apply the teachings of Belgrader and Nix to the DNA analysis system taught by Chan. An ordinary artisan would have been motivated to substitute the slab gel electrophoresis device in the DNA analysis system of Chan with the capillary electrophoresis device of Belgrader, since Belgrader taught that capillary electrophoresis analysis was "an attractive replacement for slab gel electrophoresis since runs can be accomplished much faster, and gel casting and manual sample loading are eliminated (page 3, column 2)." When substituting the slab gel electrophoresis device in the DNA analysis system of Chan with the capillary electrophoresis device of Belgrader, an ordinary artisan also would have been motivated to

further modify the resulting DNA analysis system to include a gel filtration device, since Nix taught that gel filtration devices were useful for removing salts and buffers from samples prior to capillary electrophoresis. An ordinary artisan would have recognized from these teachings of Nix that including a gel filtration device in the DNA analysis system resulting from the combined teachings of Chan and Belgrader would have improved the quality of the data obtained during use of the apparatus. An ordinary artisan would have had a reasonable expectation of success in making these modifications, since Chan expressly taught that the disclosed apparatus could be customized such that the three subsystems comprising the apparatus (*i.e.* the extraction subsystem, the amplification subsystem, and the electrophoresis subsystem) could be removed to permit updating and/or expansion (see abstract and page 5).

It also would have been *prima facie* obvious for one of ordinary skill in the art at the time of invention to perform routine experimentation to determine the optimal concentrations of the proteinase and buffer present in the extraction solution. As noted in MPEP 2144.05, "Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. '[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.'" *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). In this case, no evidence has been presented to suggest that the selection of the claimed concentrations of proteinase was other than routine or that the use of a DNA analysis system having the claimed concentration of proteinase produces unexpected results. Therefore, an ordinary artisan would have been motivated to conduct routine experimentation to determine the optimal concentration of proteinase for use in

the DNA analysis system resulting from the combined teachings of Chan, Belgrader, and Nix with a reasonable expectation of success.

Likewise, it also would have been *prima facie* obvious for one of ordinary skill in the art at the time of invention to program the microcontroller in the DNA analysis system of Chan to obtain any desired temperature incubation profile. Since Chan expressly taught that the program parameters should be determined by the user, an ordinary artisan would have been motivated to program the microcontroller of Chan to conduct any thermal cycling protocol known to be useful for conducting nucleic acid extraction and amplification reactions (*e.g.* the thermal cycling protocols recited in claims 69-74) with a reasonable expectation of success. In this case, an ordinary artisan would have been motivated to optimize the thermal cycling program in order to obtain a protocol suitable for the desired template and having the desired balance between reaction efficiency and accuracy. Thus, the apparatus of claims 58-65, 67-74, and 79-82 is *prima facie* obvious in view of the combined teachings of the cited references in the absence of secondary considerations.

9. Claim 66 is rejected under 35 U.S.C. 103(a) as being unpatentable over Chan et al. (WO 2000/60362 A1; cited on the IDS filed on December 31, 2008) in view of Belgrader et al. (Laboratory Research and Automation (1997) 9: 3-7; cited previously) as evidenced by the ABI Prism 310 Genetic Analyzer User's Manual (1998; cited previously) and further in view of Nix et al. (US 6,402,950 B1) and further in view of Uhlen et al. (US 5,330,914; newly cited).

The combined teachings of Chan, Belgrader as evidenced by the ABI Prism 310 Genetic Analyzer User's Manual, and Nix result in the apparatus of claims 58-65, 67-74, and 79-82, as discussed above.

These references do not teach or suggest that the system includes a waste valve and a valve for controlling the flow of liquid through the tube as required by claim 66.

Uhlen teaches an apparatus for purifying extra-chromosomal DNA (see abstract, column 2, line 40 – column 3, line 60, and Figure 1). The apparatus of Uhlen comprises a gel filtration column having a valve that controls the flow of liquid through the gel filtration column and a waste valve (see Figure 1 and column 2, line 40 - column 3, line 60).

It would have been *prima facie* obvious for one of ordinary skill in the art at the time of invention to incorporate any gel filtration device (*e.g.* the gel filtration device taught by Uhlen) into the apparatus resulting from the combined teachings of Chan, Belgrader, and Nix. As noted in MPEP 2144.07, it is *prima facie* obvious to select a known material based on its suitability for the intended purpose in the absence of unexpected results. In this case, an ordinary artisan would have been recognized that any gel filtration device, *e.g.*, the gel filtration device taught by Chan, was suitable for use in the apparatus resulting from the combined teachings of Chan, Belgrader, and Nix, and therefore, would have been motivated to incorporate this gel filtration device with a reasonable expectation of success. Thus, in the absence of unexpected results, the apparatus of claim 66 is *prima facie* obvious in view of the combined teachings of the cited references.

10. Claims 75-78 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chan et al. (WO 2000/60362 A1; cited on the IDS filed on December 31, 2008) in view of Belgrader et al.

(Laboratory Research and Automation (1997) 9: 3-7; cited previously) as evidenced by the ABI Prism 310 Genetic Analyzer User's Manual (1998; cited previously) and further in view of Nix et al. (US 6,402,950 B1) and further in view of Kleparnik et al. (Electrophoresis (1998) 19: 695-700; newly cited).

The combined teachings of Chan, Belgrader as evidenced by the ABI PRISM 310 Genetic Analyzer User's Manual, and Nix result in the apparatus of claims 58-64, 67-74, and 79-82, as discussed above.

Regarding claims 75-78, as discussed above, the combined teachings of Chan, Belgrader and Nix suggest programming the controller to contain instructions for feeding a combined solution of the sample, the extraction solution, and master PCR solution through a gel filtration device.

However, these references do not suggest programming the controller and microcontroller for cycle sequencing reactions as required by claims 75-77.

Kleparnik teaches a method that comprises conducting cycle sequencing using fluorescently labeled dye terminators (see page 696). The cycle sequencing method disclosed by Kleparnik comprises 25 cycles of 96°C for 10 seconds, 50°C for 5 seconds, and 60°C for 4 minutes (page 696).

It would have been *prima facie* obvious for one of ordinary skill in the art at the time of invention to program the microcontroller in the DNA analysis system resulting from the combined teachings of Chan, Belgrader, and Nix to contain instructions for a cycle sequencing program, such as the program taught by Kleparnik. An ordinary artisan would have recognized from the teachings of Chan at pages 20-21 that the disclosed DNA analysis system could be

programmed to conduct any useful DNA amplification reaction, such as the cycle sequencing reaction disclosed by Kleparnik, and therefore, would have been motivated to program the DNA analysis system to conduct this reaction, recognizing that doing so would increase the number of useful applications for the resulting apparatus. As noted in MPEP 2144.07, it is *prima facie* obvious to select a known material or method based on its suitability for the intended purpose in the absence of unexpected results. Finally, regarding the differences between the thermal cycling program suggested by the teachings of Kleparnik and the thermal cycling program recited in the claims, attention is directed to MPEP 2144.05, which states that conducting routine experimentation to determine the optimal values of results-effective variables, such as reaction temperatures and incubation times, is *prima facie* obvious in the absence of unexpected results. In this case, an ordinary artisan would have been motivated to optimize the thermal cycling program in order to obtain a protocol suitable for the desired template and having the desired balance between reaction efficiency and accuracy. It is noted that no evidence has been presented to suggest that the selection of the claimed thermal cycling conditions was other than routine or that the results obtained from such conditions should be considered unexpected compared to the closest prior art. Thus, the apparatus of claims 75-78 are *prima facie* obvious in view of the combined teachings of the cited references.

Response to Arguments

11. Applicant's arguments filed on December 31, 2008 have been considered, but they are moot in view of the new grounds of rejection presented above.

Conclusion

12. No claims are currently allowable.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Krakowski et al. (Nucleic Acids Research (1995) 23(23): 4930-4931) teaches a method that comprises conducting cycle sequencing using fluorescently labeled dideoxynucleotides, purifying the resulting products by gel filtration and analyzing the resulting products by capillary electrophoresis (pages 4930-4931).

Applicant's amendment and submission of an Information Disclosure Statement on December 31, 2008 under 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p) necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a) and MPEP § 609.04(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANGELA BERTAGNA whose telephone number is (571)272-8291. The examiner can normally be reached on M-F, 7:30 - 5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

amb

/GARY BENZION/
Supervisory Patent Examiner, Art Unit 1637